Osteoclast-like Giant Cell Tumor of the Pancreas Associated with Cystadenocarcinoma

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Osteoclast-like Giant Cell Tumor of the Pancreas Associated with Cystadenocarcinoma

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Summary

Osteoclast-like giant cell tumor is a very rare type of pancreatic malignancy, and no more than 20 cases have been reported in the English literatures. A case of this tumor associated with cystadenocarcinoma is reported. This giant cell is undistinguishable on light microscopy from osteoclast of bone and correct diagnosis of this unusual tumor is important because of its relatively poor prognosis.

Introduction

The incidence of pancreatic cancer is increasing in Japan[12]. Among the pancreatic cancer, ductal adenocarcinoma represents 81% of the autopsy series and 80% of the surgical material[14]. This paper reports a case of primary osteoclast-like giant cell tumor of the pancreas associated with cystadenocarcinoma with a brief survey of the literature.

Case Report

A 44-year-old female was admitted on September 2, 1986 with a chief complaint of palpable tumor in her left upper quadrant of the abdomen. She had experienced her symptom for last one year.

On physical examination, it was found that the abdomen was soft, but a smooth, partly lobulated, child-head-sized round mass was palpable in the left upper quadrant. No tenderness was elicited with palpation.

Her past history included appendectomy and hypertension 20 and 2 years before her ad-

Key words: Carcinoma of pancreas, Osteoclast-like giant cell carcinoma of pancreas, Pleomorphic giant cell carcinoma of pancreas, Cystadenocarcinoma of pancreas, Carbohydrate antigen 19-9.
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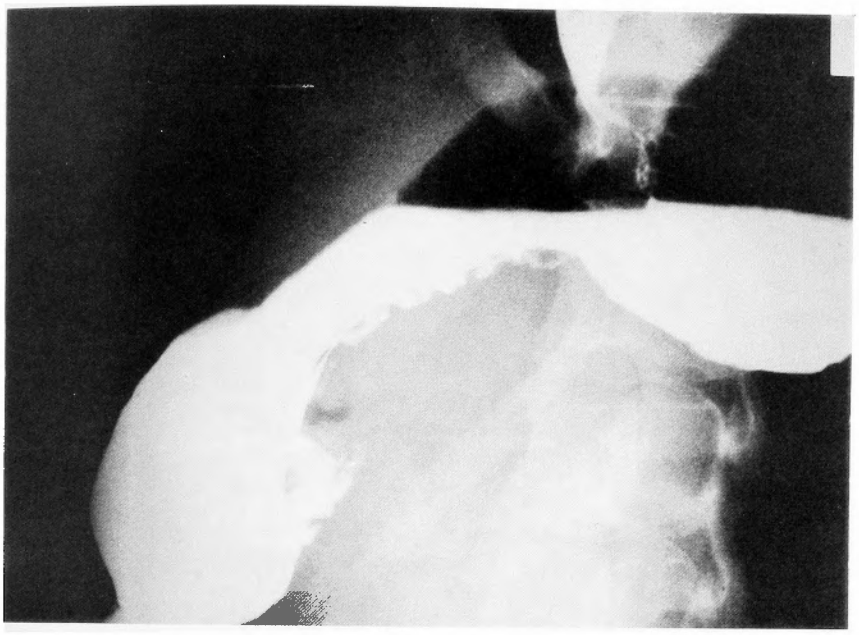

Fig. 1. An upper GI series showing evidence of cephalo-ventral displacement of the stomach.

mission, respectively. Medication was reserpine.

Laboratory results were as follows; RBC count $458\times10^4/mm^3$, WBC count $7,400/mm^3$, Hb 14.8 g/dl, hematocrit 41.2%, platelet count $41.2\times10^4/mm^3$, amylase 62 IU/l, lactate dehydrogenase 96 U/l, SGOT 21 U/l, SGPT 15 U/l, alkaline phosphatase 96 U/l, γ-GTP 21 U/l, total bilirubin 0.5 mg/dl, ferritin level 273.3 ng/ml, carcinoembryonic antigen (CEA) level 1.6 ng/ml, α-fetoprotein level 0.3 ng/ml, tissue polypeptide antigen (TPA) level 36.5 U/l, and carbohydrate antigen (CA) 19–9 level 10.2 U/ml.

An upper GI series showed evidence of cephalo-ventral displacement of the stomach (Fig. 1). An ultrasonography revealed a multiloculated mass with a strong posterior wall echo. An endoscopic retrograde cholangiopancreatography (ERCP) demonstrated narrowing and stretching of the main pancreatic duct at the tail of pancreas and no communication between the ductal system and cystic lesion. A CT scan showed a multilocular cystic mass suspected of the pancreas in origin (Fig. 2).

At laparotomy, a child-head-sized lobulated cystic mass was found arising from the tail of the pancreas. No liver metastases were recognized. Distal pancreatectomy was done. The resected specimen weighed 1,400 g and showed macroscopically a globular form with a conical protrusion (Fig. 3). Cut section examination showed various size of cystic cavities (Fig. 3). The contents of these cysts were thick and mucoid, and brownish in colour. In one of these mass, which corresponded to the neck of the protrusion shown in Fig. 3, a solid focus 2 cm in diameter was present. The content obtained from the cysts was analysed as follows: 18,000 ng/ml for ferritin, 80 ng/ml for CEA, 2.1 ng/ml for α-fetoprotein, >3,000 U/l for TPA and >12,000 U/ml for CA 19–9.

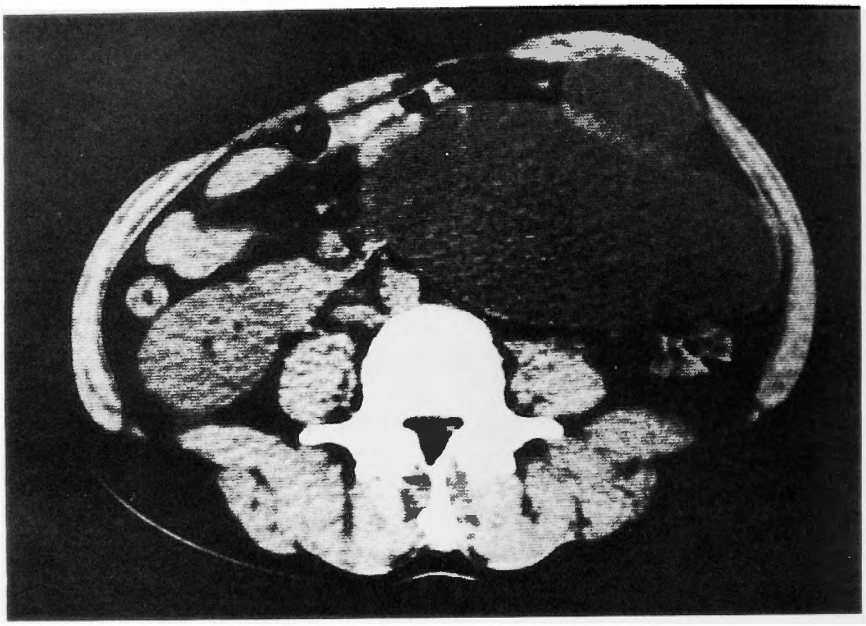

Fig. 2. A CT scan suggesting a multilocular cystic mass originating from the pancreas.

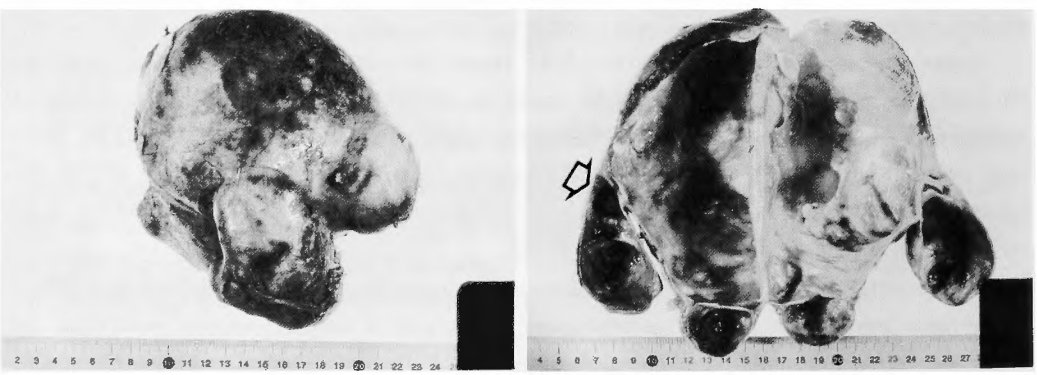

Fig. 3. The resected specimen (left), and the cut surface (right). An arrow showing a solid tumor locating at the neck of the conical protrusion.

The patient recovered uneventful and was discharged from the hospital on the 23th post-operative day. She has been doing well 3 years after surgery.

Microscopical Findings

In large part of the cystic wall, the columnar epitherial lining cells were well oriented to their basement membrane, were regularly aligned, and had no evidence of anaplasia, piling up, or invasiveness (Fig. 4). These cells were secreting mucus, which stained positively with periodic acid—Schiff stain and positively with alcian blue. In some areas, the epithelium merged with a more atypical epithelium with nuclear stratification (Fig. 4). The solid part had the appear-

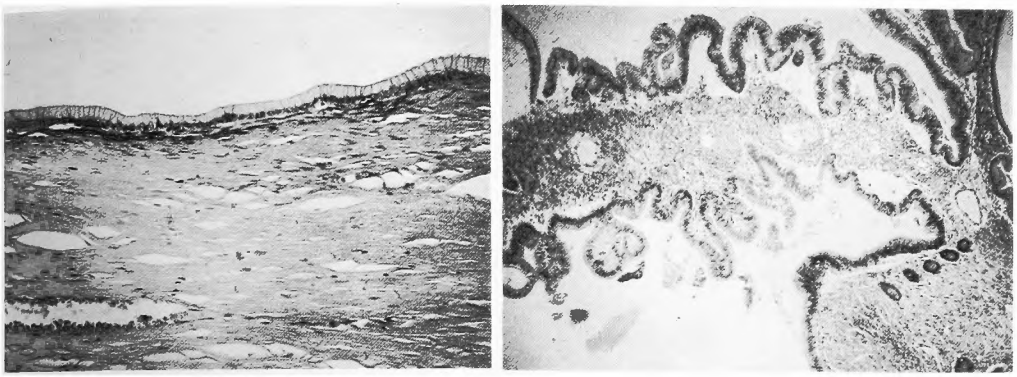

Fig. 4. Microscopical findings of the cystic wall. No malignant cells are seen (left, hematoxylin and eosin stain, ×300), but in some areas, a more atypical epithelia are observed (right, hematoxylin and eosin stain, ×150).

ance of giant cell tumor of bone (Fig. 5). It consisted of two types of cell; osteoclast-like cells and mononuclear stromal cells. The multinucleate giant cells appeared benign, and were intimately associated with the storomal cells. They contained many central nuclei. The cytoplasm was abundant and eosinophilic, and vacuolated in some giant cells. The stromal cells were oval or spindle-shaped. They had round to oval vesicular nuclei and eosinophilic cytoplasm, and showed a variable amount of nuclear pleomorphism. As shown in Fig. 6, the malignancy of the

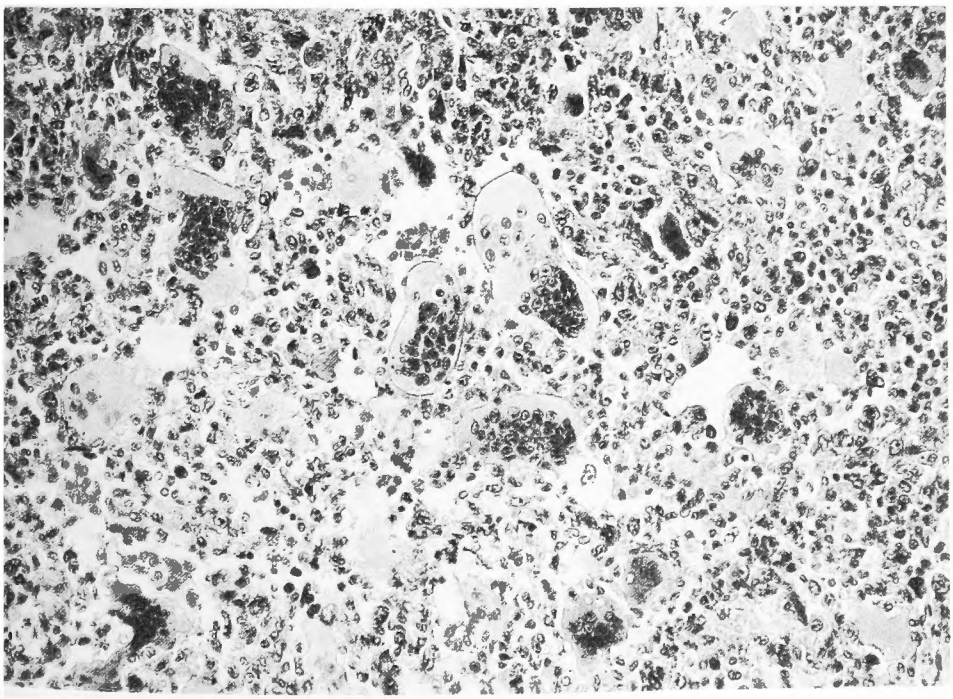

Fig. 5. Microscopical views of the solid part having the appearance of osteoclast-like giant cell tumor of bone (hematoxylin and eosin stain, ×300).

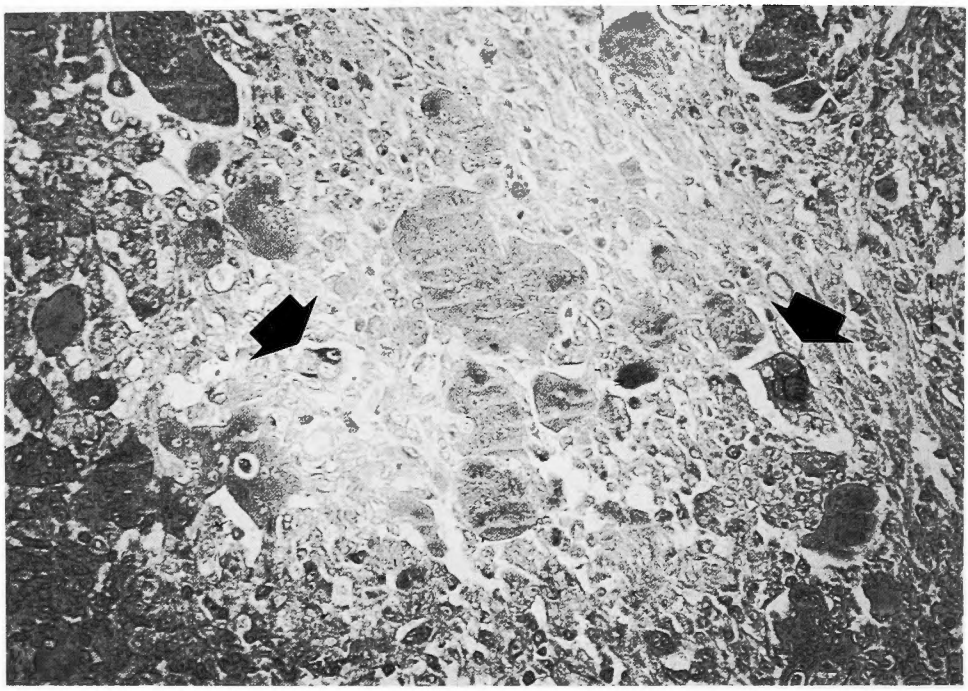

Fig. 6. CEA tissue staining showing positivity for some stromal cells (arrows, ×300).

stromal cells was partly demonstrated by the results of immunohistochemical staining of CEA activity[13].

From the above findings, the diagnosis of osteoclast-like giant cell tumor of the pancreas associated with cystadenocarcinoma was made.

Discussion

There are two types of giant cell tumor of the pancreas[1]. One is pleomorphic carcinoma, a varient of adenocarcinoma, first reported by SOMMER et al[21], and the other giant cell tumor reported by ROSAI[17]. The former is a pleomorphic giant cell carcinoma composed of malignant mononucleated and multinucleated giant cells with sarcomatous stroma and usually showing mucin secretion. The latter is a more benign-appearing giant cell carcinoma composed of osteoclast-like giant cells and malignant stroma. These two types should be strictly distinguished because the nomenclature remains nonstandardized and considerable confusion still exists.

Tumor containing osteoclast-like giant cells have been reported to occur in the thyroid[20], subcutaneous tissue[18], ovary[23], breast[7], and skin[2] as well as in the pancreas. These giant cells are indistinguishable from osteoclasts of bone[24]. Some authors[3,9] state that osteoclast-like giant cell tumor of the pancreas is apt to present as a large mass, and metastatic spread is slow, and that the prognosis seems to be musch better than in ordinary carcinoma or pleomorphic giant cells.

Table 1. Literature review of osteoclast-like giant cell carcinoma of the pancreas.

Case	Authors	Age (yrs) and sex	Symptoms	Duration of symptoms	Location	Size (cm)	Treatment	Survival
1	Shamblin, et al[19] (1966)	49, M	Periumbilical cramping pain, Anorexia	Several weeks	Head	Man's fist	Total pancreatectomy	Alive, 15 yrs later
2	Rosai[17], (1968)	82, F	Anorexia, Fatigue, Weight loss, Left upper abd. mass	1 mo.	Tail	13×12×8	Subtotal pancreatectomy, Partial gastrectomy, Splenectomy, Removal of tumor thrombi from portal vein	Alive, 4 mo. later
3	Rosai[17], (1968)	74, F	Anorexia, Weight loss, Melena	5 mo.	Head	10.5×7.5×4	Whipple	Alive, 10 mo. later
4	Kay, et al[10] (1969)	43, M	Weakness	3 mo.	Head	6×5×5	Whipple	Alive, 21 mo. later
5	Freud[6], (1973)	32, F	Nausea, Vomiting, Right upper abd. pain, Jaundice	3 mo.	Head	15 in diameter	Whipple	1 yr
6	Alguacil-Garcia, et al[1] (1977)	93, F				Large	Abdominal exploration, Biopsy	10 mo.
7	Robinson, et al[16] (1977)	63, M				15 in diameter	Radiation	4.5 mo.
8	Cubilla, et al[4] (1979)	45, M			Head	7×6	Whipple	4 yrs
9	Posen[15], (1981)	45, F	Menorrhagia, Weakness, Lower abd. pain, Nausea, Vomiting		Body	14 in diameter		
10	Trepeta, et al[22] (1981)	68, M	Back and abd. pain, Intermittent mental confusion	2 mo.	Tail	8×8×6	No (Radiation planned)	3 mo.
11	Yamashita, et al[25] (1982)	70, M	Constipation, Abd. fullness	2 yr.	Body	Thumb-tip	No	7 wk.
12	Walts[24], (1983)	59, F	Epigastric pain	3 mo.	Head and body	Large	Cholecysto-jejunostomy, Radiation, Chemotherapy	2.5 yrs
13	Jeffrey, et al[9] (1983)	55, M	Jaundice, Fever, Weight loss	2 wk.	Head	10 in diameter	Cholecysto-jejunostomy	7 mo.

14	Jalloh[8], (1983)	72, F	Upper abd. and back pain	6-8 mo.	Head	6.5×6×5	No	10 days
15	Kodama, et al[11] (1983)	59, M			Body			4 mo.
16	Kodama, et al[11] (1983)	65, M			Body			5 mo.
17	Drexler, et al[5] (1986)	75, M	Anorexia, Weight loss	4 mo.	Head	12×10	Debulking (242g), Cholecysto-jejunostomy, Gastro-jejunostomy, Radiation, Chemotherapy	5 mo.
18	Baniel, et al[3] (1987)	65, F	Abd. pain, Epigastric fullness, Constipation	3 yr.	Body	23×16×9	Local resection, Subtotal gastrectomy, Splenectomy	Alive, 6 yrs later
19	Authors, (1989)	44, F	Abd. mass	1 yr.	Tail	15×15×11	Distal pancreatectomy, Splenectomy	Alive, 3 yrs later

As listed in Table 1, up to 1988, 18 cases of this type of tumor have been reported in English literature[1,3-6,8-11,15-17,22,24,25]. There were 10 men and 9 women ranging in age from 32 to 93 with a median age of 60.9. Main clinical symptoms before admission included abdominal pain in 7, weight loss in 5, anorexia in 4 etc. Duration of these symptoms ranged from 2 weeks to 3 years (mean 8.4 months). The tumor arose from the head of the pancreas in 8, body in 5, tail in 3 and head and body in 1. The lesions were resected in only half of the patients. The average survival was only 22.3 months. Distant metastases are reported to occur in liver[8,9,22], lung[4,16] and adrenal gland[8], and the patient died, extremely speaking, 10 days after presentation[8]. From these facts, it is difficult to say the tumor slow growing or unlikely to metastasize. Even in the resected cases[4,8,10], which were pancreas head in origin, there were no obvious characteristics in clinical symptoms and macroscopic findings of the tumors compared with an ordinary adenocarcinoma of the pancreas. Thus, an early diagnosis of this type of tumor seemed to be very difficult and development of some newer diagnostic tools including CT scan and magnetic resonance imaging (MR-I) are desirable. Immunohistochemical staining of CEA activity was partly positive in our case. In general, clear demonstration of CEA activity is highly suggestive of malignancy or, possibly, premalignant change, however, this is not specific for osteoclast-like giant cell tumor of the pancreas.

Recent histological studies have revealed that these osteoclast-like cells are epithelial in origin[3,16] although some arthors consider as acinar cell[17] or stromal cell[8]. As Posen[15] proposed, the association of a cystadenocarcinoma with a giant cell tumor of the pancreas suggests that both these tumors arose from pancreatic ductal epithelium, a theory that appears to be borne

out by the fact that these two tumors were not distinctly separate but appeared to merge. Our case may support the POSEN's theory.

Surgery has been used for treatment. In fact, surgical resection in toto is the treatment of choice. When the tumor is unresectable, only bypass operation is performed as prophylaxis against intestinal obstruction or obstructive jaundice. This palliative surgery is followed by chemotherapy and/or radiation therapy, however, there has been discussion of the pros and cons of radiation. DREXLER et al[5] stated that a combination of 5-fluorouracil and radiation therapy was the first medical treatment with a document response. On the other hand, ROBINSON et al[16] reported that the lesion had not responded to radiation therapy but had spread diffusely. Thus, accurate histological recognition of the osteoclast-like tumor encourages an agressive surgical approach in view of the expectation of better prognosis.

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和文抄録

膵嚢胞腺癌に合併した破骨細胞型巨細胞癌

和歌山県立医科大学消化器外科教室
青木 洋三，谷村 弘，森 一成，児玉 悦男，植阪 和修，
川口 富司，杉本 恵洋，内山 和久，佐々木政一，上田 耕臣，
川嶋 寛昭

膵悪性腫瘍のうちでも破骨細胞型巨細胞癌は極めて稀で，1988年までの報告例は20例に満たない．我々は44歳，女性で，膵嚢胞腺癌に合併した本症を経験した．膵尾側切除術を施行し，術後約3年を経た現在，再発なく社会復帰している．

膵巨細胞癌は，病理組織学的には多形細胞型と破骨細胞型に分類され，前者の予後は極めて悪いと報告されているが，後者も，今回著者らが調べ得た範囲では，診断確定後，あるいは術後の平均生存は約22カ月に過ぎず，必ずしも良好とはいえない．本症の組織発生については，腺房細胞説と腺管上皮細胞説が挙げられているが，本例が嚢胞腺癌組織中に混在・発生していたことから，我々は後者を支持したい．